

TMI/DAG:lam 11/03/03
PATENT

Attorney Reference Number 4239-61302
Application Number 10/017,372

LISTING OF CLAIMS

This listing of claims will replace all prior versions and listings of claims in the application:

1. **(Currently amended)** A functional TGF- β 1 ~~family-fusion~~ protein, comprising:
a functionalizing peptide tag of no more than about 100 amino acids for detecting, quantifying, or providing a specific additional function to the fusion protein; and
a mature TGF- β 1 ~~family-protein~~ comprising residues 279-283 and 296-408 of SEQ ID NO: 37, or an amino acid sequence that has at least 95% sequence identity with ~~the mature TGF- β family protein residues 279-283 and 296-408 of SEQ ID NO: 37~~ and which retains TGF- β 1 ~~family-protein~~ activity;
wherein the functionalizing peptide tag is inserted between a pair of adjacent residues between about residues positions 1 and 22 of the mature ~~portion of the~~ TGF- β 1 ~~family~~ protein;
and wherein the activity of the TGF- β 1 fusion protein is reduced by no more than 50% as compared to the mature TGF- β 1 ~~family-protein~~.
2. **(Currently amended)** A functional TGF- β 1 ~~family-protein~~ dimer formed by the association of two of the fusion proteins of claim 1.
3. **(Original)** The dimer of claim 2, wherein the dimer is a homodimer.
4. **(Currently amended)** The dimer of claim 2, made by a process comprising:
expressing a nucleic acid molecule in a eukaryotic cell to produce a monomer fusion protein, wherein the nucleic acid molecule comprises:
a sequence encoding the functionalizing peptide tag;
a sequence encoding the mature TGF- β 1 ~~family-protein~~; and
a sequence encoding a pro-region (latency associated peptide) of the TGF- β 1 ~~family-protein~~, located to provide targeting and/or assembly and/or processing of the fusion protein encoded for by the nucleic acid.

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5. **(Original)** The dimer of claim 4, wherein the process further comprises:
associating two monomer fusion proteins to form the dimer.

6. **(Currently amended)** The dimer of claim 4, wherein the sequence encoding the pro-region is located upstream to both the sequence encoding the functionalizing peptide tag and the sequence encoding the mature TGF- β 1-family protein.

7. **(Original)** The dimer of claim 4, wherein the process further comprises:
cleaving the pro-region (latency associated peptide) from at least one fusion monomer.

8. **(Original)** The dimer of claim 4, wherein the process further comprises:
cleaving the pro-region (latency associated peptide) from both fusion monomers.

9. **(Currently amended)** The fusion protein of claim 1, wherein the functionalizing peptide tag is inserted downstream of residue five of the mature TGF- β 1-family protein.

10. **(Cancelled).**

11. **(Currently amended)** The fusion protein of claim 10, where the protein comprises the amino acid sequence as in the mature portion of SEQ ID NO: 37.

12-17. **(Cancelled).**

18. **(Currently amended)** The fusion protein of claim 1, further comprising a pro-region (latency associated peptide) of the TGF- β 1-family protein located to provide targeting and/or assembly and/or processing of the fusion protein.

19. **(Original)** The fusion protein of claim 18, wherein the pro-region is located at the N-terminal region of the fusion protein.

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20-27. (Cancelled)

28. (Previously presented) The fusion protein of claim 1, wherein the tag is an epitope tag, a purification tag, or an identification tag.

29. (Previously presented) The fusion protein of claim 1, wherein the tag comprises a FLAG tag, a c-myc tag, a 6x His tag, a HA tag, a Tat tag, a T7 tag, a GFP peptide, or a GST peptide.

30. (Cancelled).

31. (Currently amended) ~~The~~ An isolated nucleic acid molecule encoding the fusion protein of claim ~~30~~1, comprising ~~a sequence comprising~~ residues 845-1234 of SEQ ID NO: 36.

32. (Currently amended) The isolated nucleic acid molecule of claim ~~30~~31, further comprising a sequence encoding a TGF- β pro-region.

33. (Currently amended) The isolated nucleic acid molecule of claim 32, comprising ~~a sequence comprising~~ SEQ ID NO: 36.

34. (Currently amended) A recombinant nucleic acid molecule comprising a promoter sequence operably linked to the isolated nucleic acid molecule according to claim ~~30~~31.

35. (Currently amended) An isolated transgenic cell comprising a recombinant nucleic acid molecule according to claim 34.

36. (Original) The transgenic cell of claim 35, wherein the cell is a bacterial cell or an eukaryotic cell.

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37. (Original) The eukaryotic cell of claim 36, wherein the cell is a yeast cell or a mammalian cell.

38-57. (Cancelled).

58. (Currently amended) A TGF- β family fusion protein, comprising:
a N-terminal region consisting of an amino acid sequence of a pro-region (latency associated peptide) of a TGF- β 1-family protein,
a functionalizing peptide tag of no more than about 100 amino acids; and
an amino acid sequence consisting of the mature portion of the TGF- β 1-family protein;
wherein the functionalizing peptide tag is inserted between a pair of adjacent residues between about residues 1 and 22 of the mature portion of the TGF- β 1-family protein;
and wherein the portion of the fusion protein comprising the mature portion of the TGF- β 1-family protein and the functionalized peptide tag has a TGF- β 1-family protein activity that is reduced by no more than 50% as compared to the mature TGF- β 1-family protein alone.

59. (New). An isolated nucleic acid molecule encoding the fusion protein of claim 1, comprising residues 835-1197 of SEQ ID NO: 8, SEQ ID NO: 10, residues 835-1197 of SEQ ID NO: 12, SEQ ID NO: 14, residues 845-1222 of SEQ ID NO: 32, residues 849-1226 of SEQ ID NO: 34, or residues 845-1234 of SEQ ID NO: 38.

60. (New). An isolated nucleic acid molecule encoding the fusion protein of claim 18, comprising SEQ ID NO: 8, 12, 32 or 38.

61. (New) The fusion protein of claim 1, where the protein comprises the amino acid sequence as in the mature portion of SEQ ID NO: 9, 11, 13, 15, 33 or 39.